

Robust ordering of independent components and analysis of event-related functional magnetic resonance imaging data

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Abstract: Independent Component Analysis (ICA) was used to decompose the fMRI time series signal and separate the BOLD signal change from the structured and random noise. Rather than using component analysis to identify spatial patterns of activation and noise, the approach we took was to identify ICA components contributing primarily to the noise. These noise components were identified using an algorithm that examines the Fourier decomposition of each component time series. ICA revealed significant treatment of both structured and random noise. Nevertheless, this technique suffers from a fundamental limitation of not providing a consistent ordering of the signal components. This mandates human intervention to pick out the relevant activation components from the outcome of ICA, which poses a significant obstacle to the practicality of this technique. In this work, a simple yet robust technique is proposed for ranking the resultant independent components. This technique adds a second step to ICA based on WN criterion modified as well as power spectral analysis. The proposed technique is verified using computer simulations as well as actual real event-related functional magnetic resonance imaging data from a healthy human volunteer and the results confirm the practicality and robustness of the proposed method. This power spectral technique as a post processing leads to provide a consistent and reproducible ordering of independent components and to isolate the noise components of the MR signal by ranking the result and correlating the data with the activation stimulus paradigm, noise components were then subject to be removed before subsequent reconstruction of the time series data.

Keywords: Functional magnetic resonance imaging, independent components analysis, white noise criterion, spectral analysis, signals de-noising.

I. INTRODUCTION

Functional MRI (fMRI) based on BOLD contrast has evolved into a leading technique for functional brain imaging due to its noninvasiveness, high spatial resolution, and relatively high temporal resolution. One of the most challenging aspects of fMRI is the extraction of the BOLD signal from the complicated susceptibility-weighted (T^*) MR signal. Various noise sources contribute to the complexity of this susceptibility-weighted signal. Those physiologic in origin include MR signal modulation due to respiration, the beating of the human heart, and gross subject movement. These physiological sources can modulate the susceptibility, apparent proton densities, and apparent relaxation times. Other potential noise sources are scanner instability leading

to signal drift, signal oscillations, and other complex image artifacts. The advent of functional magnetic resonance imaging (fMRI) has resulted in many exciting studies that have exploited its unique capability. It provides a valuable noninvasive tool for investigating brain function. The different magnetic properties of oxy- and deoxy-hemoglobin are used to visualize localized changes in blood flow, blood volume and blood oxygenation in the brain [1, 2, and 3]. These in turn become indicators for local changes in neural activity. To observe these hemodynamic changes, the subject is exposed to controlled stimuli, which are carefully designed to affect only certain brain functions then rapid acquisition of a series of brain images is performed. The sequence of images is analyzed to detect such changes and the result is expressed in the form of a map of the activated regions, which represents sensory, motor, and cognitive functions in the brain [4]. fMRI analysis approaches range from model-based to exploratory, although model-based approaches are by far the most utilized [5]. Model-based approaches are extremely useful when the time course of the hemodynamic response can be inferred apriori, however the hemodynamics of the brain are still being studied and good a priori assumptions are sometimes not available [6]. Besides, the data are in general very noisy, and much statistical research has been devoted to studying how the weak activation signals may be extracted with optimal sensitivity. Thus, the use of data-driven analysis in fMRI is inherently attractive because it does not rely on imposed assumptions about experimental conditions. The concept of data driven decompositions became familiar since principal component analysis (PCA) and independent component analysis (ICA) have been introduced to fMRI data analysis [7, and 8]. Both ICA and PCA are closely related to projection pursuit methods [9]. The underlying idea is to find interesting directions or components within the multi-dimensional data set. Both ICA and PCA use linear transformation to get the components of the observed signals [10]. The key difference however, is in the type of components obtained. The goal of PCA is to obtain principal components, which are defined as the uncorrelated direction of highest variance. In ICA however, the stronger constraint of statistical independence is imposed. It seeks to obtain statistically independent components. Hence, PCA algorithms use only second order statistical information, while ICA algorithms utilize higher order statistical information for separating the signals. Moreover, PCA gives projections of the data in the direction of the maximum variance. The principal components (PCs) are ordered in terms of their variances: the first PC defines the direction that captures the maximum variance possible; the second PC defines (in the remaining orthogonal subspace) the direction of maximum variance, and so forth. This provides a natural ranking for the resulting components (even though this might not provide information about the usefulness of the components since the variance of a signal is not necessarily related to the importance of the variable). On the other hand,

ICA involves an intermediate whitening step that does not make the ranking based on projection magnitude possible. Therefore, there is no consensus of how this ordering can be performed [11]. Several attempts were reported including the use of the value of higher order statistics; these methods were not proven useful in many applications including fMRI and electro physiology data [12]. The lack of consistent ordering of components results in different arrangement of independent components each time the analysis is performed even on the same data set, which mandates the intervention by the user to select the “interesting” components out of the analysis result. This is usually a cumbersome task that takes fairly long time and makes the technique subject dependent. Therefore, an analysis technique that would allow the robust ordering of independent components without the intervention of the user would be rather useful. In the present work, we present a simple yet effective method for functionally ranking the resulting components of the ICA algorithm by using the power spectrum analysis creating a new nature ranking not depend on any model-based fMRI tools, as other but depends on the nature of the data itself, applying to the outcome of ICA. This new technique enables the elimination of the limitations of other techniques and provides a robust model-free mechanism for analyzing fMRI data. The proposed technique is verified using computer simulations as well as actual real event-related functional magnetic resonance imaging data from a healthy human volunteer and the results confirm the practicality and robustness of the proposed method. This power spectral technique as a post processing leads to provide a consistent and reproducible ordering of independent components and isolate the random noise components of the MR signal by ranking the result and Noise components were then can be removed before subsequent reconstruction of the time series data.

II. THEORY

1) Independent Component Analysis

Independent Component Analysis is a signal processing technique, created to separate a number of statistically “independent” sources that have been mixed linearly without further knowledge of their distributions or dynamics.

ICA assumes there are N statistically independent inputs that have been mixed linearly in N output channels. Knowledge of joint distributions and statistical independence of latent variables is assumed [13].

If the matrix M represents the fMRI time series data in each voxel, then the decomposition can be thought of in terms of the matrix equation

$$M = WC \quad (1)$$

where W is the mixing matrix and C is the matrix containing the component map voxel values. In general, one wishes to solve for Z in the equation $C = ZM$, where Z is the inverse matrix of W and is a square matrix of full rank. Each column of Z^{-1} ($=W$) returns the time course of modulation of its corresponding component map. These time courses may be correlated and non-orthogonal, but the distributions of voxel values in C are as statistically independent as possible. The ICA algorithm determines Z by an iterative method based on information theory principals, and the matrices C and Z provide a linear decomposition of the fMRI data.

There are two types of ICA that can be calculated: spatial ICA, in which the spatial components are constrained to be independent ($C = ZM$), and temporal ICA, in which the time courses of modulation are constrained to be independent ($C = ZM'$)[14].

2) WN criterion

In order to determine which components of the decomposition can be considered white noise, we utilize an observed property of power spectra estimated by the multitaper method. Empirically have observed that if the power spectrum of a time series of random white noise is estimated by a straightforward Fourier transform with only one taper, the mean power across all frequency bins of the power spectrum is approximately equal to or greater than the standard deviation of the power across all frequency bins of the power spectrum. In the case of multitaper spectral estimation, in which there is a reduction in variance, one finds that the standard deviation of the power across all frequency bins of the power spectrum is frequently less than the mean power across all frequency bins of the power spectrum [14]. The WN criterion was met if the mean power across all frequency bins of the power spectrum was greater than the standard deviation of the power across all those frequency bins. If for any given component, the WN criterion was met, then its power spectrum was considered essentially the spectrum of white noise and that component was scored as a relevant contributor to the overall noise content of the MR signal (i.e., the corresponding time mode component was considered a “noise” component). All data sets were processed with and without this criterion. If the WN criterion was not used, then only time-series components that contributed respiration and cardiac noise were considered noise sources.

The WN criterion was also used as a method for determination of a cutoff between relevant and non-relevant components in PCA-based de-noising methods. This was defined as the point at which all components higher in rank passed the WN criterion for being non-structured (random) noise. These components were therefore labeled as non-relevant and were automatically zeroed for the data sets in which nonstructural noise was to be removed. Also, if nonstructural noise was to be considered for removal, then lower order components below the relevancy cutoff were also subjected to screening by the WN criterion.

III. METHODOLOGY

The algorithm implemented, all supporting routines were written in Matlab (math Works, Natick, MA). This approach was investigated by applying it to simulated fMRI datasets, one for event-related fMRI and the other for Block-design. In the simulation studies, the performance of the present approach was measured when it is used as a post process step after PCA/ICA to make its results easier to evaluate. In the experimental studies, the present approach was applied to activated time courses from experimental data obtained to illustrate its practical utility.

1) The computer simulations were performed whereby a computer generated ER-fMRI activation signal was added to an actual baseline data set. The number of epochs was 5 and the length of each epoch was 100. The generated activation was generated using a signal of the form (see Fig.1-3 for an example):

$$X(t) = (1 - \exp(\frac{-t}{T1}))^3 \cdot \exp(\frac{-t}{T2}) \quad (2)$$

Where T1 and T2 are constants that can be adjusted to obtain the desired shape, and t represents the sampling times (i.e., the image number within an epoch). This signal was replicated for each epoch and added to either simulated Gaussian white noise or experimentally acquired baseline data as shown in fig.1, 3. Also a computer generated Block design activation signal was added to an actual baseline data set as shown in fig.4.

2) We added functions to the fastica package as a post-processing step as shown in fig.6. These functions will be included later with our Practical implementation steps for our proposed technique [15].

3) The WN criterion observation [14]. We extended to a rank criterion with help of correlation between the activation paradigm of the data and the output of the ICA as individual component to be a new rank method for the ICA output

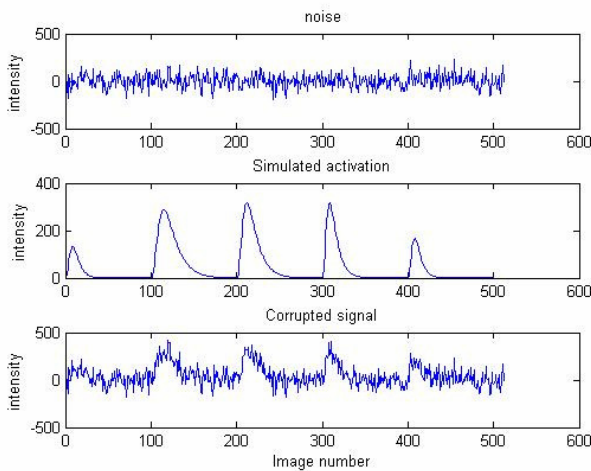


Fig.1. Simulated activation time course

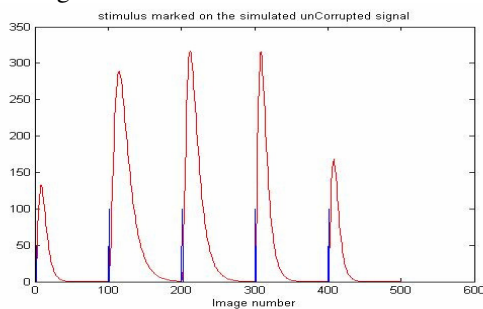


Fig.2. Stimulus (blue) marked on simulated activation (red)

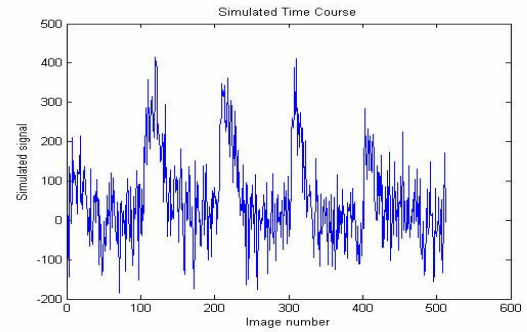


Fig.3. Computer generated ER-fMRI activation signal time course

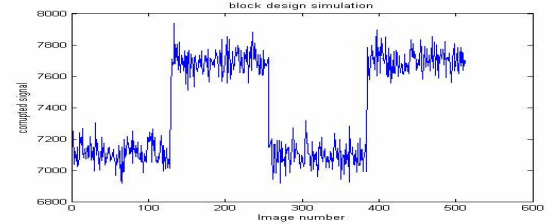
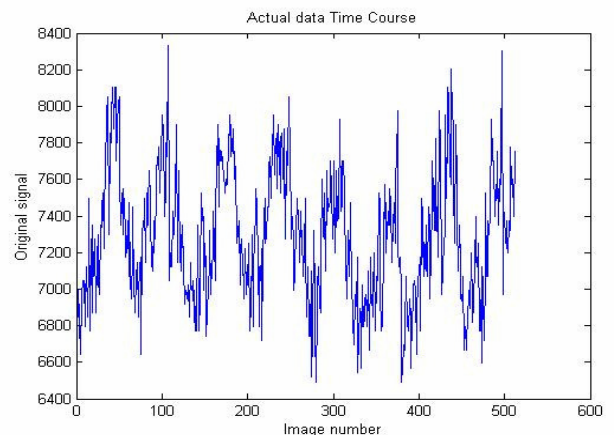
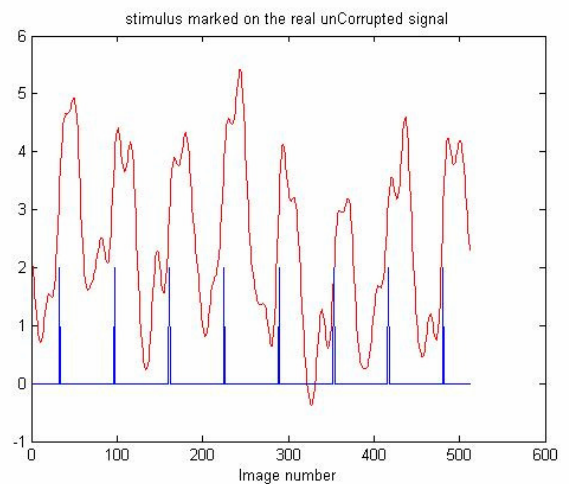


Fig.4. Computer generated Block design activation signal time course.



(a)



(b)

Fig.5. (a) actual data time course , (b) stimulus(blue) marked on the real uncorrupted signal (red)

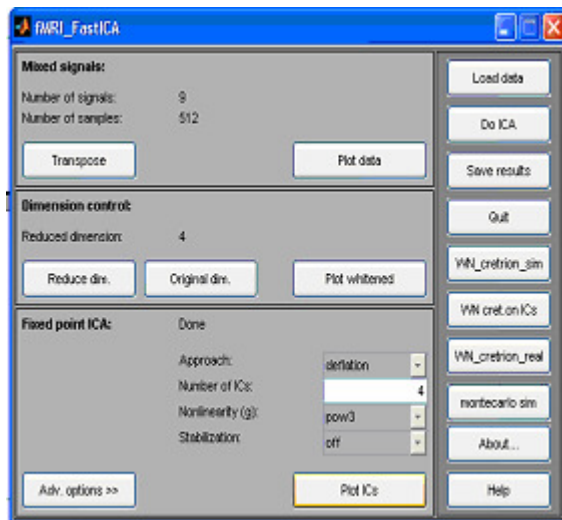


Fig.6. Functions has been added to Fastica as a Post process step

4) The activation signal seems to be our helper as from the experimental data we have the information needed to extract the stimulus paradigm activation, as we know that the subject performed rapid finger movement cued by flashing LED goggles. The study consisted of 31 epochs, with 64 images per epoch. Temporal data from only 8 epochs of pixels in both the motor and visual cortices were processed using the new method therefore the stimulus created for the correlation are shown in fig. (5-b) for the real data, and as shown in fig. 2 for the simulated data

5) Practical implementation steps

The following are the steps needed to implement the new technique:

Step 1) selects the area of interest to be examined for a real activation, 3x3 pixels at a time.

Step 2) recall the data and do PCA /ICA technique for the selected time series using fastica module the modified one [15].

Step 3) compute the mean power for the output from ICA across all frequency bins of the power spectrum.

Step 4) compute the standard deviation of the power for the output from ICA across all those frequency bins of the power spectrum.

Step 5) the power spectra of each component were evaluated with what we term the WN modified (white noise) criterion.

Step 6) divide the standard deviation over the mean as a ratio.

Step 7) search the signal for WN (white noise) criterion.

Step 8) rank the above ratio in descending order

Step 9) classify the ICA output by applying the t-test among all components of the ICA output.

Step 10) correlate the results with the actual stimulus paradigm activation and get the hypothesis, as well as the signal significances to the hypothesis,

Step 11) rank the signal according to step (6) and step (10)

Step 12) arrange the signals in descending order according to the new nature ranking created from step (11).

Step 13) the higher the value of the rank the higher the relation with the activation paradigm stimulus a certain grade assigned for each IC based on its relation with the activation paradigm and display the output as shown in fig (7-10).

Step 14) These components which classified as a noise were therefore labeled as non-relevant and were automatically zeroed for the data sets in which noise was to be removed.

Step 15) repeat the steps from 1-14 for the rest of pixels.

IV. RESULTS AND DISCUSSION

The proposed technique was verified using computer simulations as described before in methods as well as actual data from a human volunteer. The computer simulations were performed whereby a computer generated ER-fMRI activation signal was added to an actual baseline data set. The baseline data were collected on a healthy human volunteer using an EPI sequence (TE/TR = 25/500 ms) Matrix=64x64, field of view (FOV)=20 cmx20cm, slice thickness=5 mm, 640 images) on a Siemens Magnetom Vision 1.5 T clinical scanner. The number of epochs processed was 8 and the length of each epoch was 64. The generated activation was designed to include inter-epoch variations in both the magnitude and width of the activation signal in order to test the performance of the new technique in preserving such variations. The actual data were obtained from an activation study performed on a volunteer using a Siemens 1.5T clinical scanner. In this study, an oblique slice through the motor and the visual cortices was imaged using a T2*-weighted EPI sequence (TE/TR= 60/300 ms, Flip angle=55°, FOV=22cm x 22cm, slice thickness=5 mm). The subject performed rapid finger movement cued by flashing LED goggles. The study consisted of 31 epochs, with 64 images per epoch. Temporal data from only 8 epochs of pixels in both the motor and visual cortices were processed using the new method. Temporal ICA was applied to process groups of pixels within a user-specified region of interest of size 3x3. The proposed ranking method based on the new method was used to order the outcome of ICA, which came in different order each run. The results of ICA before and after applying the ordering technique are shown in Figs. 7&8 for simulated data, and fig.9 & 10 for an actual real data were obtained from an activation study performed on a volunteer using a Siemens 1.5 T clinical scanner. As can be seen, the components are consistently ordered in these examples. Furthermore, in each of these examples, even though the order of components came different from ICA from the data before the application of the proposed technique, the results after its application were exactly the same each time. This suggests that the addition of the proposed method as a post-processing step after ICA makes the technique more practical for use in clinical settings.

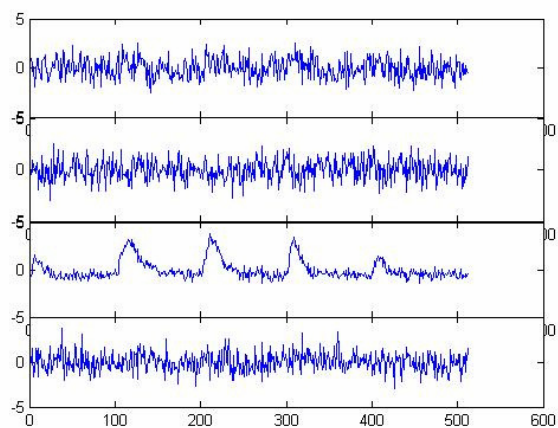
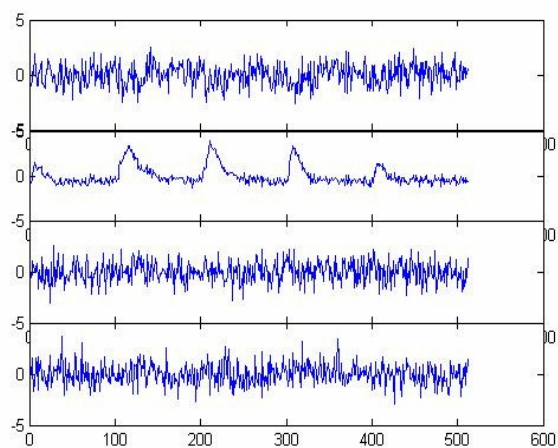
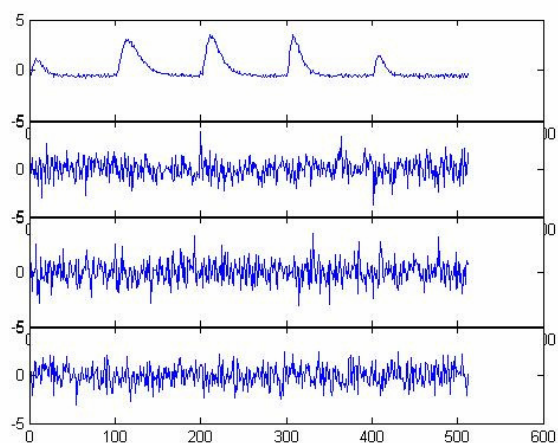


Fig.7. The generated ICS without ordering for Simulated data.

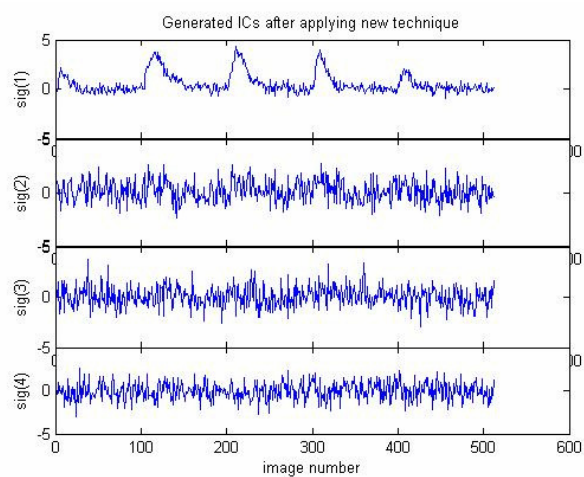
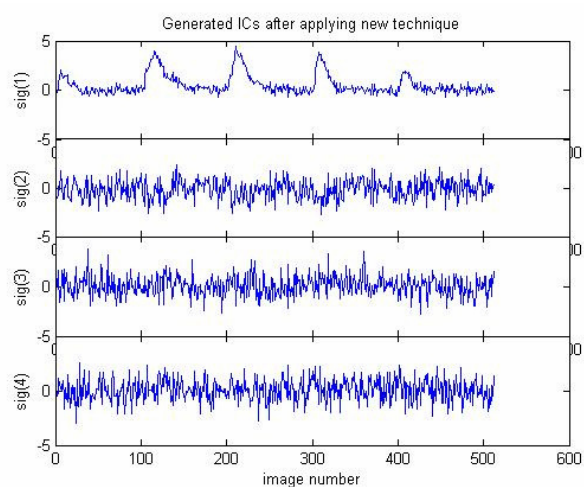
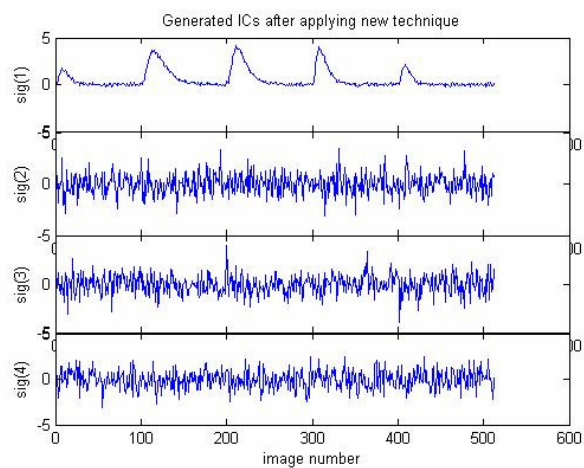


Fig.8. The generated ICS after applying the new technique ordering-for simulated data.

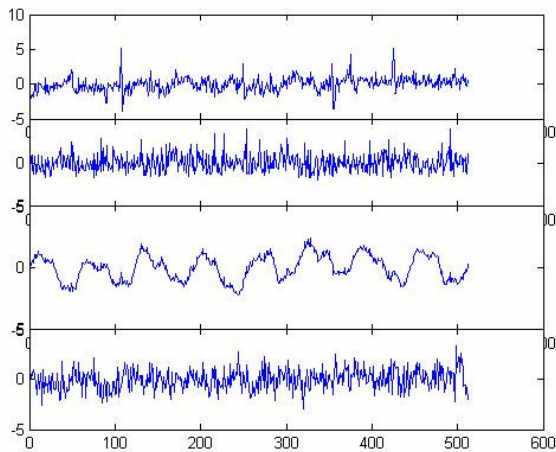
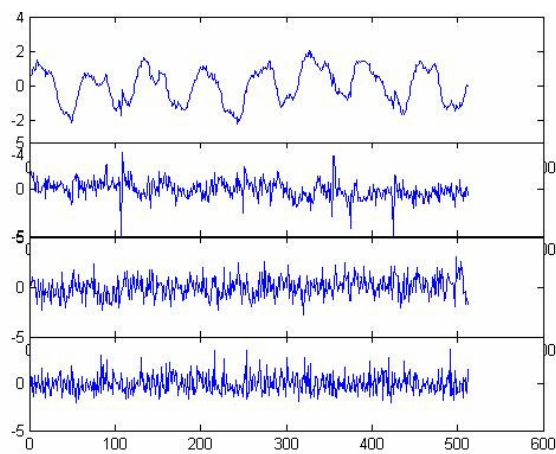
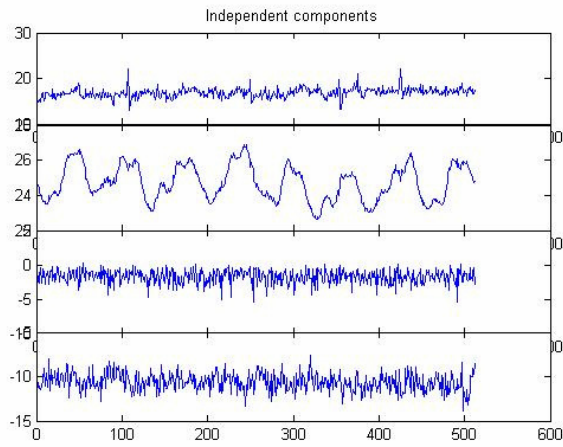


Fig.9. The generated ICS without ordering for real data.

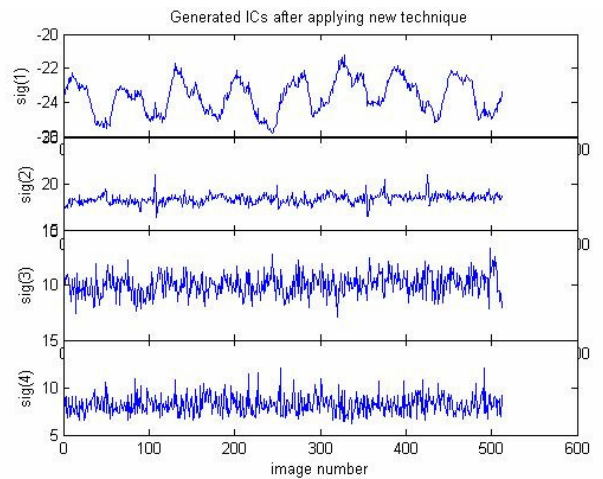
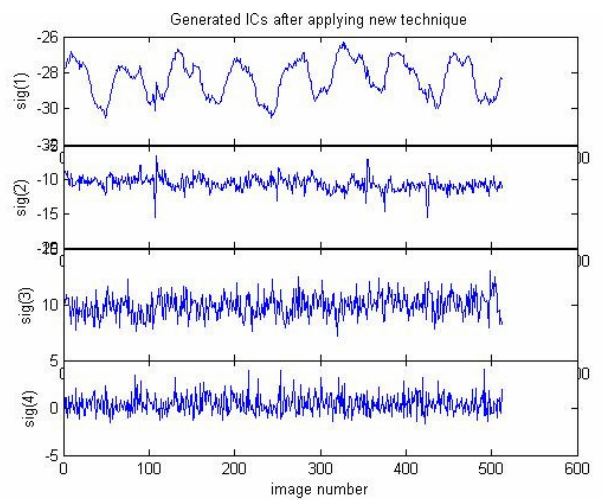
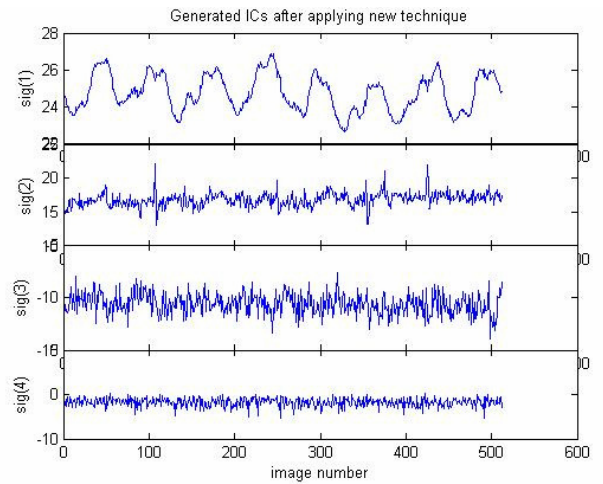


Fig.10. The generated ICS after applying the new technique ordering for real data.

V. CONCLUSION

The major implications of these results can be summarized in a few key conclusions. The most fundamental finding is that component analysis of the fMRI BOLD signal, followed by deletion of undesirable components and then reconstruction of the data, can be used successfully as a way to help separate task-related voxel variations from non-task-related "noise." We demonstrated algorithms that automatically select ICA components that are more likely to contain noise and mark them for subsequent deletion. A procedure for noise identification was tested for noise. This procedure was based on Fourier analysis of the time variation of each component's activity, followed by examination of the structure of the power spectrum. Extraction of various kinds of noise by using ICA is one of the most interesting features of the methods tested here. In all, these results seem to indicate that component-analysis-based on a natural ranking system depending on the nature of the data avoiding any assumption not like other technique depends on basis function model may lead to problems with noise especially in fMRI environment. That is mainly because noise can just by pure chance make a strong correlation with some signal in the model. So, some signal that looks like that component can deceive the system and give a very high correlation with a noisy component while results will convert this high correlation factor to high grade for this component as an activation response and gives wrong result which need applying any measurement technique to measure the similarity between the data and the model, accordingly our proposed technique might be a valuable addition to the family of post-processing techniques which are used to improve the recovery of information from the BOLD-based fMRI signal and may provide a more complete picture of the extent of each region's activation by task-related activity. As our proposed technique for ordering the outcome of temporal ICA is subjected to further correlation with the activation stimulus for the same data, also the powerful of this technique is that it does not need to correlate with all components of the output of ICA as in the CCA technique but the correlation here is between the output of ICA based in individuals basis. The results obtained in our experiments suggest this technique to be highly robust, which makes it suitable as a Post processing step after ICA to make its results easier to evaluate and the technique more practical to use.

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REFERENCES

- [1]. S. Ogawa, D.W. Tank, R. Menon, J.M. Ellermann, S.-G. Kim, H. Merkle, and K. Ugurbil, "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging," *Proc. Natl. Acad. Sci. USA* **89**, pp. 5951–5955, 1992.
- [2]. K.J. Worsley and K.J. Friston, "Analysis of fMRI time-series revisited-again," *Neuroimage* **2**, pp. 173-181, 1995.
- [3]. W.W. Orrison, J.D. Lewine, J.A. Sanders, and M.F. Hartshorne, *Functional Brain Imaging*, Mosby-Year Book, St. Louis, 1995.
- [4]. N. Lange, S. C. Strother, J. R. Anderson, F. A. Nielsen, A. P. Holmes, T. Kolenda, R. Savoy, and L. K. Hansen, "Plurality and resemblance in fMRI data analysis," *Neuroimage* **10**, pp. 282-303, 1999.
- [5]. R.L. Buckner, "Event-related fMRI and the hemodynamic response," *Hum. Brain Mapp.* **6**, pp. 373-377, 1998.
- [6]. L. K. Hansen, J. Larsen, F. A. Nielsen, S. C. Strother, E. Rostrup, R. Savoy, N. Lange, J. Sidtis, C. Svarer, and O. B. Paulson, "Generalizable patterns in neuroimaging: How many principal components?," *Neuroimage* **9**, pp. 534-544, 1999.
- [7]. J. R. Moeller and S. C. Strother, "A regional covariance approach to the analysis of functional patterns in positron emission tomographic data," *J. Cereb. Blood Flow Metab.* **11**, pp. A121-A135, 1991.
- [8]. V. Cherkassky and F. Mulier, *Learning From Data: Concepts, Theory, and Methods*, John Wiley & Sons, New York, 1998.
- [9]. J. H. Friedman, "Exploratory projection pursuit," *J. of the American Statistical Association* **82**, pp. 249-266, 1987.
- [10]. H. Hotelling, "Relations between two sets of variates," *Biometrika* **28**, 321–377, 1936.
- [11]. S. LaConte, S.-C. Ngan, and X. Hu, "Enhancing functional paradigm specific independent components with the AFRICA technique," *Proc. 2001 ISMRM Meeting*, 2001.
- [12]. A. Hyvarinen, J. Karhunen, and E. Oja, *Independent Component Analysis*, John Wiley & Sons, New York, 2001.
- [13]. O. Friman, J. Cadefam, P. Lundberg, M. Borga, and H. Knutsson, "Detection of neural activity in functional MRI using canonical correlation analysis", *Magnetic Resonance in Medicine* **45**, pp. 323-330, 2001.
- [14]. Noise Reduction in BOLD-Based fMRI Using Component Analysis ,Christopher G. Thomas*,† Richard A. Harshman,* and Ravi S. Menon†,‡,§ , *NeuroImage* **17**, 1521–1537 (2002) doi:10.1006/nimg.2002.1200
- [15]. <http://www.cis.hut.fi/projects/ica/fastica>.